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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,131	01/31/2001	Toshihiko Yamauchi	TOYAM69.001A	8649

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/762131	YAMAUCHI
	Examiner	Art Unit
	GAMBEL	1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on _____.

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-5

4a) Of the above claim(s) _____ is/are withdrawn from consideratio 1-2

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 3-5

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requireme

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disappr d by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☑ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

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PAPER NO. 11

DETAILED ACTION

1. Applicant's amendment, filed 12/30/02 (Paper No. 10), has been entered.
Claim 5 has been amended.

Claims 3-5 are under consideration in the instant application

Claims 1- 2 (and 3 and 5 as they read on the non-elected inventions) have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 12/30/02 (Paper No. 10).
The rejections of record can be found in the previous Office Action (Paper No. 7).

3. Claim 5 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed:
"wherein the administration of the substance is initiated when the number of platelets in the candidate does not decrease".

Applicant's amendment, filed 12/30/02 (Paper No. 10), asserts that no new matter has been added and directs written support to Example 2 on pages 11-12 of the instant specification.
However, the specification as filed does not provide sufficient written description or set forth the metes and bounds of this phrase. As indicated below, the recitation of the claimed "limitation" is ambiguous and indefinite. Also, the number of platelets vary in an individual including ITP patients such that initiating an antagonist when the platelets do not decrease appears to be an ever changing variable. Further, Example 2 appears to simply administer the anti-CD40L antibody in an experimental animal model. In turn, there does not seem to be sufficient guidance nor blazemarks as to the meaning and determination for the instant methods encompassing the claimed limitation "wherein the administration of the substance is initiated when the number of platelets in the candidate does not decrease", particularly the aspects of "initiation" and "the number of platelets in the candidate does not decrease". It is not clear at which stage of the disease or treatment of ITP and/or patient is being targeted by the claimed method or when the number of platelets in the candidate does not decrease. Further, the specification, including Example 2, provides support for administering an antagonist to ITP patients and not initiating the administration as a particular point. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

Applicant's arguments and amended claim 5, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

4. Claim 5 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite in the recitation "wherein the administration of the substance is initiated when the number of platelets int he candidate does not decrease" because the metes and bounds of this recitation are ambiguous and ill-defined. For example, ITP is a chronic disease. As pointed out previously, it is not clear what times or stages of the disease / patient populations are encompassed by the claims methods. For example, it appears from the specification as filed that the claims may encompass treating ITP during remission (e.g. pages 2-3, overlapping paragraph, page 8, paragraph however it is not clear that the claimed "limitation" encompasses this stage of disease. Also, the number of platelets vary in an individual including ITP patients such that initiating an antagonist when the platelets do not decrease appears to be an ever changing variable. Further, Example 2 appears to simply administer the anti-CD40L antibody in an experimental animal model; therefore the administration of anti-CD40L antibody appears to be simply administered to an ITP patient regardless of platelet count. In addition, the claimed limitations is relative in nature, which renders the claim indefinite. The limitation is not defined by the claim and the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

Applicant's arguments and amended claim 5, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

5. Claims 3-5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kalled et al. (WO 98/39026; 1449, #10) (see entire document) for the reasons of record set forth in the previous Office Action (Paper No. 8).

Applicant's arguments, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

Applicant argues that Kalled et al. does not treat teaching treating the disease state at the onset of the disease state, as required by the claimed invention.

Applicant's reliance on comparing the timing of administering anti-CD40L antibodies in the experimental models between the prior art and the examples of the instant application. However, it is clear from the specification (e.g. see page 8, paragraph 1) that the instant claims would encompass treating ITP patients during remission, which is encompassed by the prior art teaching.

Also, it is noted that the prior art teaching is consistent with the diagnosis and treatment associated with the timing of immunosuppressive therapy currently employed for ITP. See pages 197-199 of Textbook of the Autoimmune Diseases, edited by Lahita, Lippincott Williams & Wilkens, Philadelphia, 2000 and pages 920-923 of The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, edited by Beers and Berkow, Merck Research Laboratories, Whitehouse Station, NJ, 1999

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human immunoregulatory diseases such as autoimmunity or ITP targeted by the claimed invention. With respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed and treated only after significant tissue damage or the appropriate parameters have occurred.

Again, see the citations above in the Textbook of the Autoimmune Diseases and The Merck Manual of Diagnosis and Therapy concerning the standard practice of diagnosing and treating human ITP patients.

Treating NZB/NZW animal models provide experimental models of human diseases, but ITP undergoes periods of exacerbation and remission.

By its very name, ITP in humans is idiopathic. Also, ITP in humans is chronic.

It would have readily apparent to the ordinary artisan at the time the invention was made that applicant's claims and supporting disclosure was drawn to treating human ITP patients after the diagnosis of ITP, including treating at the time of remission.

Given the indefiniteness and the idiopathic and chronic nature of exacerbation and particularly remission of ITP in human patients, the prior art teaching of treating ITP patients with anti-CD40L would have anticipated the instant claims.

As pointed out previously, Kalled et al. teach methods of treating ITP (see page 2, paragraph 3; Claim 11) with anti-CD40L antibodies (see pages 6-8, Compounds and Claims). Given the teachings of administering therapeutically effective amounts of anti-CD40L antibodies on pages 9-11 in Dosages and Frequency of Treatment, it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies at the time the invention was made. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat ITP with anti-CD40L antibodies.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Applicant's arguments are not found persuasive.

6. Claims 3-5 are rejected under 35 U.S.C. § 102(e) as being anticipated by Black et al. (U.S. Patent No. 6,001,358) (see entire document) for the reasons of record set forth in the previous Office Action (Paper No. 8).

Applicant's arguments, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

Applicant argues that Black et al. does not treat teaching treating the disease state at the onset of the disease state, as required by the claimed invention. .

Applicant's reliance on the instant Examples and the examiner's rebuttal are essentially the same as addressed above in Section 5.

As pointed out previously, Black et al. teach methods of treating ITP (see column 14, line 40: column 32, line 5, lines 57-58) with anti-gp39 antibodies (see entire document). Given the teachings of administering therapeutically effective amounts of anti-gp39 antibodies in amounts to produce a therapeutic effect that can be determined by standard techniques well known to those ordinary skill in the art (e.g. column 33, paragraph 2) for therapeutic or prophylactic immunosuppression (e.g. column 34, paragraph 2-4), including inducing immunosuppression in the treatment and the prevention of diseases (e.g. column 33-34, overlapping paragraph); it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies at the time the invention was made. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat ITP with anti-gp39 antibodies.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Applicant's arguments are not found persuasive.

7. Claims 3-5 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lederman et al. (U.S. Patent No. 5,993,816) (see entire document) for the reasons of record set forth in the previous Office Action (Paper No. 8).

Applicant's arguments, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

Applicant argues that Lederman et al. does not treat teaching treating the disease state at the onset of the disease state, as required by the claimed invention. .

Applicant's reliance on the instant Examples and the examiner's rebuttal are essentially the same as addressed above in Section 5.

As pointed out previously, Lederman et al. teach methods of treating ITP (see column 11, line 33) with 5C8-specific (gp39-specific) antibodies (see entire document, including column 10, line 60 to column 11, line 35). Given the teachings of administering effective amounts of anti-5C8 antibodies to inhibit T cell activation of B cells; it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies at the time the invention was made. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat ITP with anti-5C8 antibodies.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Applicant's arguments are not found persuasive.

8. Claims 3-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kalled et al. (WO 98/39026) AND/OR Black et al. (U.S. Patent No. 6,001,358) AND/OR Lederman et al. (U.S. Patent No. 5,993,816)
in view of either one of
Nemoto et al. (Br. J. Haematol. 91: 691-696, 1995) OR
Medical Letter on Drugs and Therapeutics 39: 6-8, 1996 OR
Williams et al. (Br. J. Haematol. 101: 779 - 782, 1998).

for the reasons of record set forth in the previous Office Action (Paper No. 8).

Applicant's arguments, filed 12/30/02 (Paper No. 10), have been fully considered but are not found convincing.

Applicant argues that Lederman et al. does not treat teaching treating the disease state at the onset of the disease state, as required by the claimed invention

Applicant's reliance on the instant Examples and the examiner's rebuttal are essentially the same as addressed above in Section 5.

In response to applicant's arguments that there is no suggestion to combine the references and there is unexpected results, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the teachings of Kalled et al., Black et al. and Lederman et al. as well as Nemoto et al., Medical Letter on Drugs and Therapeutics and Williams et al. all provide and address different aspects of treating ITP and , in turn, the treatment of ITP with anti-CD40L antibodies, as it would read on treating ITP patients during exacerbation and remission of the disease to solve the same or similar problem encompassed by the claimed invention. Therefore, the prior art would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

Further, the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01 (C). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

The following of record is provided for applicant's convenience.

Kalled et al.(see entire document, including page 2, paragraph 3; Claim 11), Black et al. (see entire document, including column 14, line 40: column 32, line 5, lines 57-58) And Lederman et al. (see entire document, including column 11, line 33) are all taught above and teach treating and/or preventing ITP patients with anti-CD40L antibodies.

Given the ambiguity of the limitation recited in claim 5 "wherein the administration of the substance is initiated when the candidate's immune response to platelet begins", the additional references of Nemoto et al., Medical Letter on Drugs and Therapeutics and Williams et al. are provide to address different aspects of treating ITP and , in turn, the treatment of ITP with anti-CD40L antibodies.

Nemoto et al. teach the use of an immunosuppressant to the prevent the development of thrombocytopenia and suppress the increase in circulating antibodies against platelets in an experimental model of ITP (see entire document). Nemoto et al. teach that corticosteroids are generally applied as the first-line drug therapy for ITP and that an immunosuppressant in combination with steroids would suppress the production of antibodies and phagocytic function in treating ITP patients (see page 695, column 2, paragraph 1).

Given the immunosuppressive properties of anti-CD40L antibodies, one of ordinary skill in the art at the time the invention was made would have been motivated to provide anti-CD40L antibodies in combination with known treatments of ITP in order to inhibit and prevent immune responses to platelets in ITP patients.

Medical Letter on Drugs and Therapeutics teach Rho(D) Immune globulin as well as prednisone or IVIG and sometimes splenectomy for the treatment of both acute and chronic ITP (see pages 6-8). Platelet counts increase after treatment and maintenance treatments would be helpful. (See page 7).

Williams et al. teach FcγRIIIa polymorphisms are implicated in the pathophysiology of ITP and be responsible for modulating the immune response in this heterogenous autoimmune disease (see entire document, including Abstract and Discussion). Williams teach that platelet antigens are targeted in this disease and that the destruction of antibody sensitized platelets are involved in this disease (see Introduction).

Given the immunosuppressive properties of anti-CD40L antibodies and the use of anti-CD40L antibodies in the treatment and prevention of ITP, as taught by Kalled et al., Black et al. and Lederman et al.; one of ordinary skill in the art at the time the invention was made would have been motivated to provide said anti-CD40L antibodies to treat ITP in combination with other known treatments of ITP in order to inhibit and prevent immune responses to platelets in ITP patients, given the role of anti-platelet antibodies play in ITP. One of ordinary skill in the art would have been motivated to provide anti-CD40L antibodies in both acute and chronic ITP to prevent and control the disease manifestations of this disease, including the anti-platelet responses and the consequences of anti-platelet responses. In addition, in certain instances of the expression of certain FcγRIIIa polymorphisms, as taught by Williams (also see Discussion); one of ordinary skill in the art at the time the invention was made would have been motivated to provide anti-CD40L antibodies in certain targeted patient populations to protect against more severe disease.

One of ordinary skill in the art at the time the invention was made would have been motivated to select anti-CD40L antibodies alone or in combination with other known and practiced treatments to prevent and to treat the elaboration and consequences of anti-platelet responses in ITP patients. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
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February 20, 2003